

Identification of acute coronary syndrome via body-surface mapping and inverse electrocardiography

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Introduction

Acute myocardial infarction (AMI), commonly referred to as heart attacks, remain a leading cause of morbidity, mortality and healthcare expenditure in the United States, ranking as the fifth most expensive hospital diagnosis. Emergency departments in the United States receive 10 million annual visits for chest pain. Evaluation of these patients costs \$10-13 billion per year [1]. Unfortunately, despite the central role of the traditional electrocardiogram (ECG) in the diagnosis of AMI, the standard ECG remains limited by both a lack of sensitivity and specificity, leading to a delay in diagnosis and consequently increased mortality, morbidity, re-admission rates, and costs [2].

The cornerstone of acute MI management is rapid reperfusion therapy (either percutaneous coronary intervention (PCI) and stent placement or the administration of thrombolytic agents) to restore blood flow to the myocardium. Expeditious reperfusion reduces acute MI mortality by 50% [3]. The standard 12-lead ECG remains the foundation of rapid AMI diagnosis. Although the finding of ST elevations on the ECG is highly specific for a complete occlusion of a coronary vessel, (termed an ST-elevation MI, or STEMI), this group represents only 30% of all AMIs as seen in Fig. 1. The remaining 70% of AMIs are diagnosed by an elevation in circulating cardiac biomarkers (typically cardiac-specific troponin) indicative of myocardial necrosis.

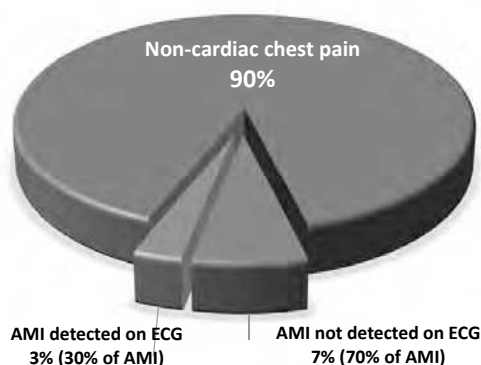


Figure 1: Although only 10% of patients with chest pain prove to have an acute MI (AMI), unfortunately 70% of these AMIs are undiagnosed on the standard ECG.

Both high-resolution body surface electrical mapping and inverse electrocardiography provide more extensive and detailed electrical information than the 12-lead ECG and, in theory, could improve AMI diagnosis. Clinical application of these methods to AMI diagnosis, however, has been limited by the lack of an appropriate bioelectric metric for acute MI, which we address in this study.

Materials and Methods

The standard ECG is fundamentally limited by poor spatial sampling and by variations in individual torso anatomy. To improve spatial sampling, additional electrodes (typically 80 or more) can be used to provide a more complete sampling of the torso electrical signals, a method termed body surface potential mapping [4]. To overcome the distorting effect of torso anatomy, patient-specific epicardial electrical potentials can be reconstructed based on body surface recordings in conjunction with a 3D model of cardiac and torso anatomy, a method termed electrocardiographic imaging (ECGI) or inverse electrocardiography [5–7].

Inverse electrocardiography improves detection of myocardial ischemia

Previous studies have demonstrated that inverse electrocardiography can accurately identify complete coronary occlusions [8]. To further explore the sensitivity of inverse solutions for sub-total occlusions (comprising 40% of NSTEMIs), raw data from experiments at the University of Utah were used (data obtained from the EDGAR database). Experiments were performed on an ex vivo canine heart suspended in a torso-shaped tank filled with electrolyte solution. Ischemia was introduced by graded reduction in blood flow in the left anterior descending artery (LAD).

Using our ECGI methods, we found epicardial potentials from the recorded canine torso surface ECGs. We used singular value decomposition to quantify T wave complexity (a marker of ischemia [9]). As shown in Fig. 2, the T wave complexity calculated from reconstructed epicardial potentials was $\sim 2 - 10\times$ more sensitive to ischemia than the same metric calculated from body surface recordings, demonstrating that inverse electrocardiography can improve ischemia detection compared to the use of body surface recordings.

ECGI has been used to study arrhythmia substrates,

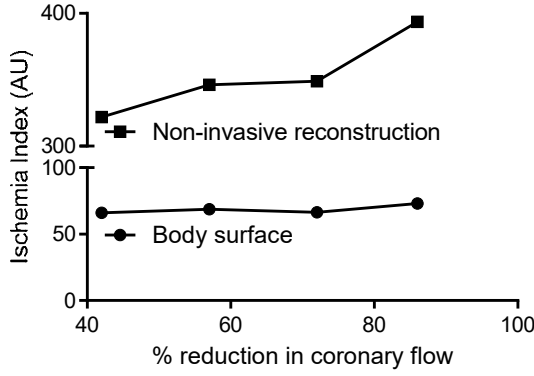


Figure 2: The ischemia index (based on T wave complexity) of reconstructed epicardial potentials (squares) is markedly more sensitive to ischemia than body surface T wave complexity (circles).

activation patterns, and repolarization changes. It has also been used to guide invasive ablation procedures targeting PVCs, atrial tachycardia, and atrial fibrillation. It has, however, not been applied to the clinical diagnosis of ischemia and infarction.

Non-Invasive Cardiac Evaluation (NICE)

Our Non-Invasive Cardiac Evaluation (NICE) system for ECGI integrates body surface recordings with mathematical reconstruction of epicardial electrical potentials and uses signal analysis of both body surface and epicardial signals to identify subtle signs of ischemia or infarction.

Our forward problem solution uses heart and torso geometry to find transfer coefficients $\mathbf{Z}_{BH}$ that relate heart to body surface potentials [10].

$$\mathbf{Z}_{BH} = -(\mathbf{P}_{BB} - \mathbf{G}_{BH}\mathbf{G}_{HH}^{-1}\mathbf{P}_{HB})^{-1}(\mathbf{P}_{BH} - \mathbf{G}_{BH}\mathbf{G}_{HH}^{-1}\mathbf{P}_{HH}), \quad (1)$$

where $\mathbf{P}$ is a matrix of solid angles and $\mathbf{G}$ is a matrix of gradient integral coefficients. Transfer coefficients were calculated using 7-point Radon numerical integration to approximate gradient integral terms [11].

Conventional estimation of heart-surface potentials using Tikhonov regularization yields $\hat{\phi}_H$ given by

$$\hat{\phi}_H = (\mathbf{Z}_{BH}^*\mathbf{Z}_{BH} + \tau\mathbf{R}^*\mathbf{R})^{-1}\mathbf{Z}_{BH}^*\phi_B, \quad (2)$$

where $\mathbf{Z}_{BH}$ are the transfer coefficients given in Eq. 1, τ is a regularization constant and $\mathbf{R}$ is a regularization matrix. $\mathbf{R} = \mathbf{I}$, the identity matrix, is known as zero-order Tikhonov regularization and is commonly used in the literature as a basis for comparison of regularization techniques.

Our NICE system comprises a) recording body surface signals from 120 electrodes b) construction of a 3D model of

torso and heart anatomy and c) ECGI to reconstruct epicardial electrical signals. The overall feasibility of the technique is demonstrated by the accurate reconstruction of the known pattern of electrical activation in the normal heart [12], as shown in Fig. 3.

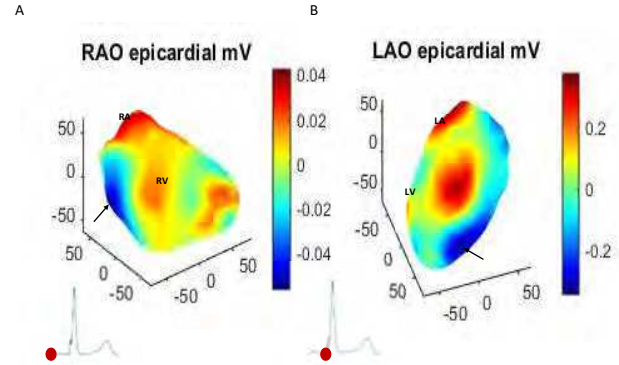


Figure 3: NICE accurately reconstructs normal cardiac electrical patterns. Local negative potentials reflect activation breakthrough to the epicardial surface. A. Site of earliest atrial activation (arrow) occurs near the sinus node at the time of the body surface P wave onset (inset). B. Site of the earliest ventricular activation (arrow) occurs on the infero-lateral LV wall at the onset of the body surface QRS (inset). Both locations are consistent with prior mapping studies. RA=right atrium, RV=right ventricle, LA=left atrium, LV=left ventricle, RAO=right anterior oblique view, LAO=left anterior oblique view.

Detection of myocardial infarction in Emergency Department patients using NICE

NICE was performed on ten subjects who had presented to the Barnes-Jewish Hospital Emergency Department in St. Louis, MO, USA, with chest pain concerning for a cardiac etiology and both the body surface recordings and the reconstructed epicardial potentials were analyzed. Patient-specific data were distilled into a score reflecting the probability of a heart attack. On clinical follow up, five of the participants had abnormal troponin elevation and five did not.

Results

Analysis of 10 subjects with NICE identified two promising metrics of acute MI (as defined by troponin elevation). The first, based on an analysis of body surface activation times and termed the "activation index," demonstrates a greater dispersion of activation time in subjects with elevated troponin (Fig. 4A), a finding likely corresponding to the known delay in activation in the context of myocardial ischemia [13].

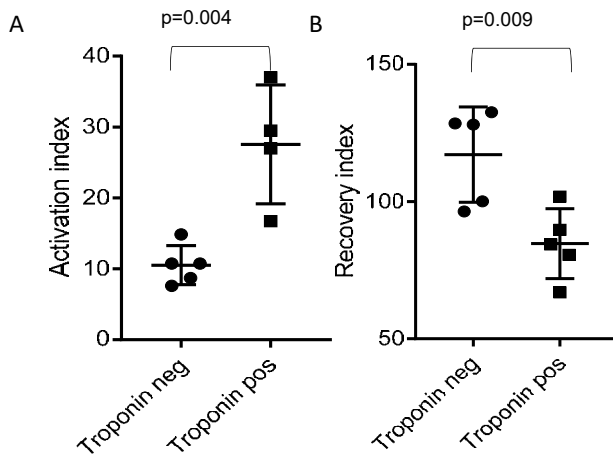


Figure 4: A. Patients with elevated troponin exhibit an increased dispersion of activation as measured on the body surface. B. Patients with elevated troponin also exhibit evidence of abnormal recovery as measured in reconstructed epicardial potentials. Both activation and recovery indices were significantly different ($p < 0.05$) when separated according to troponin assay results.

Notably, four of the five troponin-positive patients lacked a focal coronary lesion and, consistent with the predicted result, the dispersion of recovery ("recovery index") was significantly reduced in troponin-positive patients (Fig. 4B).

Discussion

Ischemia is known to affect myocardial recovery by shortening the action potential [13]. Depending on the spatial pattern of ischemia, this effect is predicted to either increase or decrease the dispersion of recovery. Localized transmural ischemia causing local action potential shortening is predicted to increase the dispersion of repolarization. In contrast, global sub-endocardial ischemia, by shortening the sub-endocardial action potentials which are normally longer than mid-myocardial and sub-epicardial action potentials [14], is predicted to reduce the transmural dispersion of repolarization. Notably, four of the five troponin-positive patients lacked a focal coronary lesion and, consistent with the predicted result, the dispersion of recovery ("recovery index") was reduced in troponin-positive patients (Fig. 4B).

Conclusions

Our results demonstrate promising metrics which permit accurate discrimination between troponin positive and negative patients without the delay required for biomarker elevation. Importantly, the differences between groups are not only statistically significant, but are sufficiently separated that an appropriate threshold value can be identified which would provide useful positive and negative predictive values.

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Acknowledgments

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